

L4
1-12Apts
own work

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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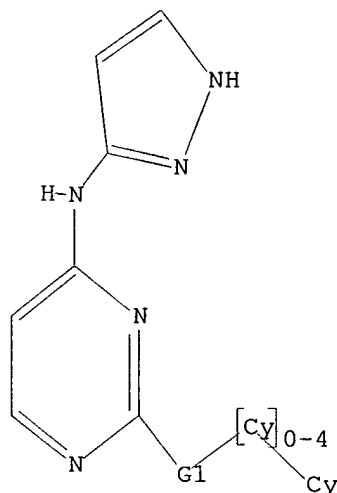
Uploading 10026966.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



G1 C, O, S, N, Cl, Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 16:46:12 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 43 TO ITERATE

100.0% PROCESSED 43 ITERATIONS

16 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 467 TO 1253

PROJECTED ANSWERS: 80 TO 560

L2 16 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 16:46:26 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 913 TO ITERATE

100.0% PROCESSED 913 ITERATIONS
SEARCH TIME: 00.00.01

243 ANSWERS

L3 243 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

148.15

148.36

FILE 'CAPLUS' ENTERED AT 16:46:32 ON 28 MAR 2003

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE COVERS 1907 - 28 Mar 2003 VOL 138 ISS 14
FILE LAST UPDATED: 27 Mar 2003 (20030327/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3

L4 15 L3

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:615605 CAPLUS

DOCUMENT NUMBER: 137:169539

TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Golec, Julian M. C.; Miller, Andrew; Knegt, Ronald

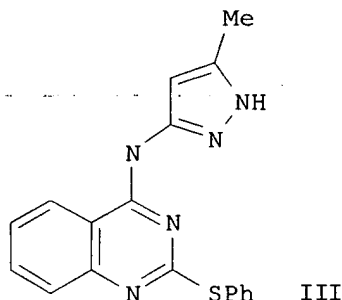
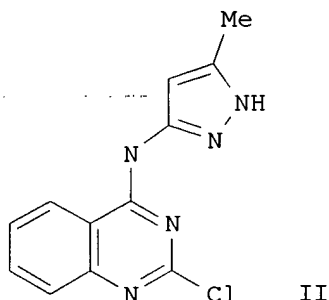
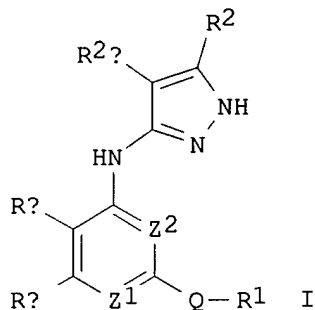
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 335 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 14
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062789	A1	20020815	WO 2001-US51031	20011219
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WO 2002066461	A1	20020829	WO 2001-US49139	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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US 2003004161	A1	20030102	US 2001-26975	20011219
US 2003036543	A1	20030220	US 2001-25164	20011219
US 2003055068	A1	20030320	US 2001-26967	20011219
US 2003004164	A1	20030102	US 2001-34683	20011220
US 2003022885	A1	20030130	US 2001-34019	20011220
PRIORITY APPLN. INFO.:			US 2000-257887P	P 20001221
			US 2001-286949P	P 20010427
OTHER SOURCE(S):			MARPAT 137:169539	
GI				



AB 285 Title compds. I [wherein Z1 = N or CR8; Z2 = N or CH; and at least 1 of Z1 and Z2 = N; Rx and Ry = independently TR3 or LZR3; or C2RxRy = (un)substituted fused (hetero)cycle; Q = NR4, O, S, C(R6')2, 1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R1 = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, or carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR4, CO, CONH, NHCO, SO2, SO2NH, NHSO2, CO2, OCO, OCONH, or NHCO2, with provisos; Z = alkylidene chain; L = O, S, SO, SO2, NR6SO2, SO2NR6, NR6, NR6CO, NR6CO2, NR6CONR6, NR6SO2NR6, NR6NR6, OCONR6, or W; R2 and R2a = independently R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, COR, CO2R, CO(CH2)0-1COR, NO2, CN, SO0-2R, N(R4)2, carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R = independently H or (un)substituted aliph., (hetero)aryl, or heterocyclyl; R4 = independently R7, COR7, carboxy, CON(R7)2, or SO2R7; W = CO, CO2, CONR6, C(R6)2O, C(R6)2SO0-2, C(R6)2SO2NR6, C(R6)2NR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:MNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, or C(R6)2NR6CONR6; R6, R6', R7 = independently H or aliph.; or N(R6)2 or N(R7)2 = independently heterocyclyl or heteroaryl; or C(R6')2 = carbocycle; R8 = R, halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2] were prepd. However, the claims pertain only to 3-(2-amino-4-pyrimidinylamino)-1H-pyrazoles, i.e. Z1 = Z2 = N, and Q = NH. I are protein kinase inhibitors, esp. of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 .mu.M: GSK-3.beta. (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases assocd. with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

IT **446881-34-1P**, N4-(5-Cyclopropyl-1H-pyrazol-3-yl)-N2-(1H-indazol-5-

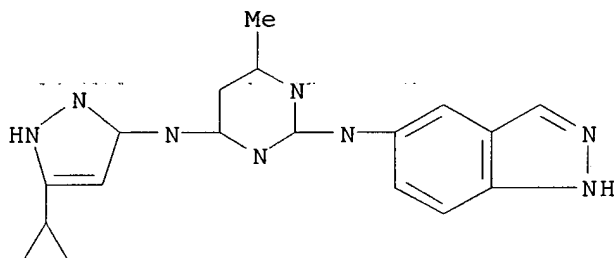
yl)-6-methylpyrimidine-2,4-diamine **446881-35-2P**,
N2-Benzothiazol-6-yl-N4-(5-cyclopropyl-1H-pyrazol-3-yl)-6-methylpyrimidine-2,4-diamine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 446881-34-1 CAPLUS

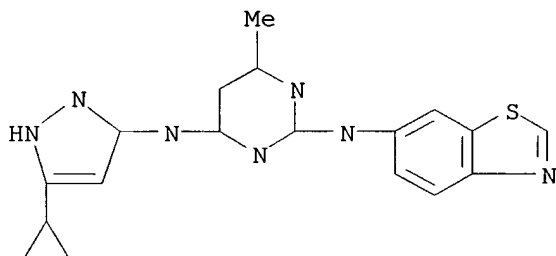
CN 2,4-Pyrimidinediamine, N4-(5-cyclopropyl-1H-pyrazol-3-yl)-N2-1H-indazol-5-yl-6-methyl- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 446881-35-2 CAPLUS

CN 2,4-Pyrimidinediamine, N2-6-benzothiazolyl-N4-(5-cyclopropyl-1H-pyrazol-3-yl)-6-methyl- (9CI) (CA INDEX NAME)

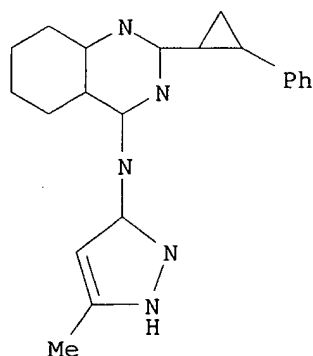


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IT **438203-20-4P**, (5-Cyclopropyl-1H-pyrazol-3-yl)[2-(3-methoxycarbonylphenylsulfanyl)quinazolin-4-yl]amine **438203-23-7P**, [2-(4-Acetamidophenylsulfanyl)-7-methoxyquinazolin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-25-9P**, [2-(4-Acetamidophenylsulfanyl)-7-hydroxyquinazolin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-28-2P**, [2-(4-Acetamidophenylsulfanyl)-7-nitroquinazolin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-38-4P**, [2-(4-Acetamidophenylsulfanyl)-6-(4-methoxyphenyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-43-1P**, [6-Methoxycarbonyl-2-(4-propionylaminophenylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438204-86-5P** **438204-90-1P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; prepn. of (pyrimidinylamino)pyrazoles as



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:575069 CAPLUS

DOCUMENT NUMBER: 137:109292

TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Davies, Robert; Golec, Julian; Kay, David; Knegt, Ronald; Patel, Sanjay

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 337 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059111	A2	20020801	WO 2001-US51120	20011219
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WO 2002066461	A1	20020829	WO 2001-US49139	20011219
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WO 2002068415 A1 20020906 WO 2001-US50312 20011219

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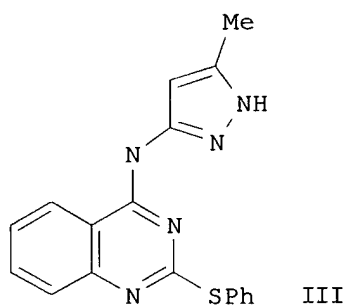
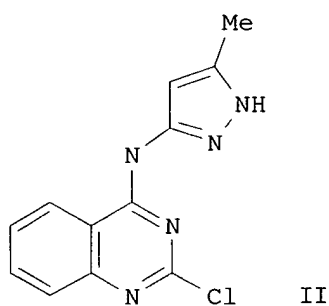
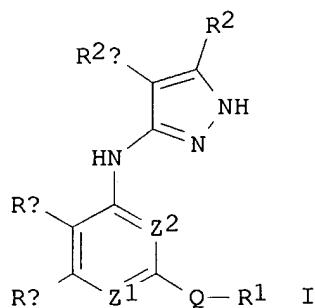
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US 2003004161 A1 20030102 US 2001-26975 20011219
 US 2003036543 A1 20030220 US 2001-25164 20011219
 US 2003055068 A1 20030320 US 2001-26967 20011219
 US 2003004164 A1 20030102 US 2001-34683 20011220
 US 2003022885 A1 20030130 US 2001-34019 20011220

PRIORITY APPLN. INFO.: US 2000-257887P P 20001221
 US 2001-286949P P 20010427

OTHER SOURCE(S): MARPAT 137:109292

GI



AB Title compds. I [wherein Z¹ = N or CR₈; Z² = N or CH; and at least 1 of Z¹ and Z² = N; R_x and R_y = independently TR₃ or LZ_{R3}; or C₂R_xR_y = (un)substituted fused (hetero)cycle; Q = NR₄, O, S, C(6a)₂, 1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R₁ = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, or

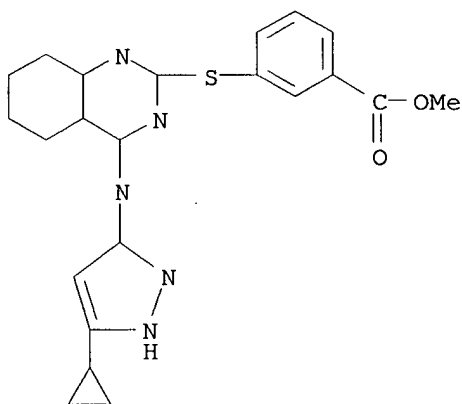
carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR4, CO, CONH, NHCO, SO2, SO2NH, NHSO2, CO2, OCO, OCONH, or NHCO2, with provisos; Z = alkylidene chain; L = O, S, SO, SO2, NR6SO2, SO2NR6, NR6, NR6CO, NR6CO2, NR6CONR6, NR6SO2NR6, NR6NR6, OCONR6, or W; R2 and R2a = independently R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, COR, CO2R, CO(CH2)0-1COR, NO2, CN, SO0-2R, N(R4)2, carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R = independently H or (un)substituted aliph., (hetero)aryl, or heterocyclyl; R4 = independently R7, COR7, carboxy, CON(R7)2, or SO2R7; W = CO, CO2, CONR6, C(R6)2O, C(R6)2SO0-2, C(R6)2SO2NR6, C(R6)2NR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, or C(R6)2NR6CONR6; R6, R6a, R7 = independently H or aliph.; or N(R6)2 or N(R7)2 = independently heterocyclyl or heteroaryl; or C(R6a)2 = carbocycle; R8 = R, halo, OR, COR, CO2R, COCOR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2] were prepd. I are protein kinase inhibitors, esp. of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 .mu.M: GSK-3.beta. (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases assocd. with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

IT 438203-20-4P 438203-23-7P 438203-25-9P
438203-28-2P 438203-38-4P 438203-43-1P
438204-86-5P 438204-90-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-20-4 CAPLUS

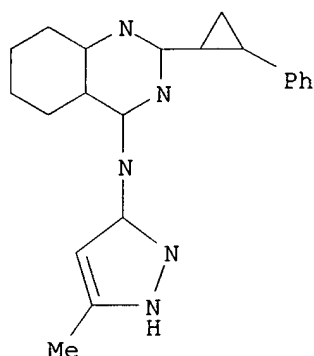
CN Benzoic acid, 3-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 438203-23-7 CAPLUS

CN Acetamide, N-[4-[[7-methoxy-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

L4 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:555487 CAPLUS

DOCUMENT NUMBER: 137:125169

TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3

INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Golec, Julian; Miller, Andrew; Knegt, Ronald

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 333 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002057259	A2	20020725	WO 2001-US49401	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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WO 2002068415	A1	20020906	WO 2001-US50312	20011219

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US 2003004161	A1	20030102	US 2001-26975	20011219
US 2003036543	A1	20030220	US 2001-25164	20011219
US 2003055068	A1	20030320	US 2001-26967	20011219
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US 2003022885	A1	20030130	US 2001-34019	20011220

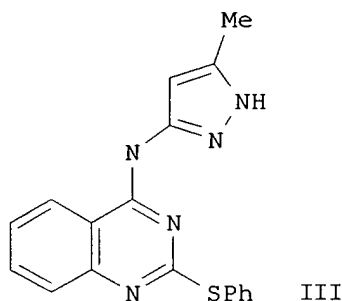
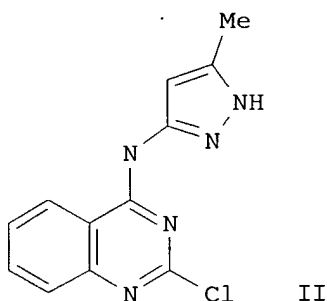
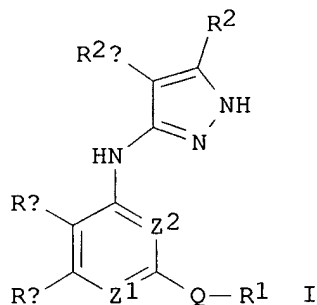
PRIORITY APPLN. INFO.:

US 2000-257887P P 20001221

US 2001-286949P P 20010427

OTHER SOURCE(S): MARPAT 137:125169

GI



AB The title compds. I [Z1 = N, CR8; Z2 = N, CH; and at least one of Z1 and Z2 = N; Rb, Rc = TR3, LZR3; C2RbRc = (un)substituted fused (hetero)cycle; Q = NR4, O, S, etc.; R1 = TD; D = (un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, carbocyclyl; T = a bond, alkylidene (un)interrupted by O, S, NR4, CO, etc.; Z = alkylidene; L = O, S, SO, SO2, etc.; R2, R2a = R, TWR6, or C2R2R2a = (un)substituted fused (hetero)cycle; R3 = R, halo, OR, etc.; R = H, (un)substituted aliph., (hetero)aryl, heterocyclyl; R4 = R7, COR7, SO2R7, etc.; W = CO, CO2, CONR6, etc.; R6, R7 = H, alkyl; or N(R6)2 or N(R7)2 = heterocyclyl, heteroaryl] were prepd.

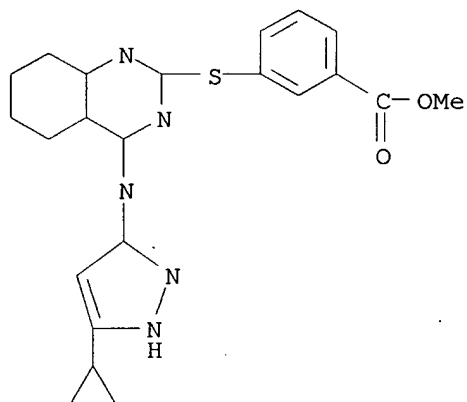
For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in tert-BuOH to give III. In bioassays, I inhibited the following kinases with K_i values reported $< 20 \mu\text{M}$: GSK-3 β . (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases assocd. with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

IT 438203-20-4P 438203-23-7P 438203-25-9P
438203-28-2P 438203-38-4P 438203-43-1P
438204-86-5P 438204-90-1P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(protein kinase inhibitor; prepn. of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-20-4 CAPLUS

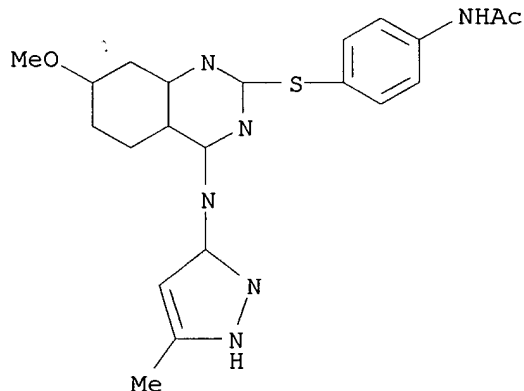
CN Benzoic acid, 3-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)

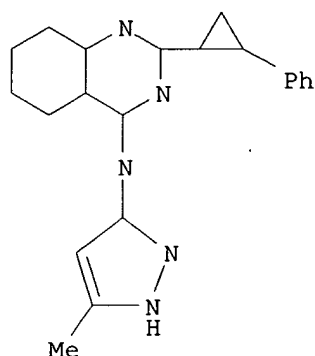


*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 438203-23-7 CAPLUS

CN Acetamide, N-[4-[[7-methoxy-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]thio]phenyl]- (9CI) (CA INDEX NAME)





*** FRAGMENT DIAGRAM IS INCOMPLETE ***

L4 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:487556 CAPLUS

DOCUMENT NUMBER: 137:47221

TITLE: Preparation of 3-(4-pyrimidinylamino)-1H-pyrazoles as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Bebbington, David; Charrier, Jean-Damien; Davies, Robert; Everitt, Simon; Kay, David; Knegt, Ronald; Patel, Sanjay

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 342 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050065	A2	20020627	WO 2001-US49140	20011219
WO 2002050065	A3	20021024		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2002068415 A1 20020906 WO 2001-US50312 20011219

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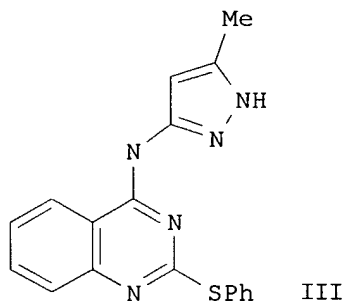
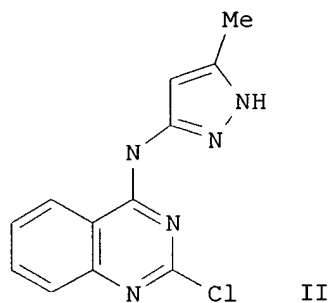
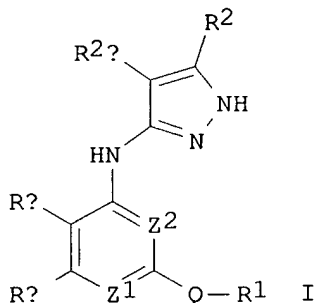
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US 2003004161 A1 20030102 US 2001-26975 20011219
 US 2003036543 A1 20030220 US 2001-25164 20011219
 US 2003055068 A1 20030320 US 2001-26967 20011219
 US 2003004164 A1 20030102 US 2001-34683 20011220
 US 2003022885 A1 20030130 US 2001-34019 20011220

PRIORITY APPLN. INFO.: US 2000-257887P P 20001221
 US 2001-286949P P 20010427
 WO 2001-US49140 W 20011219

OTHER SOURCE(S): MARPAT 137:47221

GI



AB Title compds. I [wherein Z1 = N or CR8; Z2 = N or CH; and at least 1 of Z1 and Z2 = N; Rx and Ry = independently TR3 or LZR3; or C2RxRy = (un)substituted fused (hetero)cycle; Q = NR4, O, S, C(6a)2, 1,2-cyclo(prop/but)anediyl, or 1,3-cyclobutanediyl; R1 = TD; D =

(un)substituted mono- or bicyclic (hetero)aryl, heterocyclyl, or carbocyclyl; T = a bond or alkylidene chain (un)interrupted by O, S, NR₄, CO, CONH, NHCO, SO₂, SO₂NH, NHSO₂, CO₂, OCO, OCONH, or NHCO₂, with provisos; Z = alkylidene chain; L = O, S, SO, SO₂, NR₆SO₂, SO₂NR₆, NR₆CO, NR₆CO₂, NR₆CONR₆, NR₆SO₂NR₆, NR₆NR₆, OCONR₆, or W; R₂ and R_{2a} = independently R, TWR₆, or C₂R₂R_{2a} = (un)substituted fused (hetero)cycle; R₃ = R, halo, OR, COR, CO₂R, CO(CH₂)₀₋₁COR, NO₂, CN, SO₀₋₂R, N(R₄)₂, carbamoyl, sulfamoyl, OCOR, acylamino, hydrazino, ureido, etc.; R = independently H or (un)substituted aliph., (hetero)aryl, or heterocyclyl; R₄ = independently R₇, COR₇, carboxy, CON(R₇)₂, or SO₂R₇; W = CO, CO₂, CONR₆, C(R₆)₂O, C(R₆)₂SO₀₋₂, C(R₆)₂SO₂NR₆, C(R₆)₂NR₆, C(R₆)₂NR₆CO, C(R₆)₂NR₆CO₂, CR₆:NNR₆, CR₆:NO, C(R₆)₂NR₆NR₆, C(R₆)₂NR₆SO₂NR₆, or C(R₆)₂NR₆CONR₆; R₆, R_{6a}, R₇ = independently H or aliph.; or N(R₆)₂ or N(R₇)₂ = independently heterocyclyl or heteroaryl; or C(R_{6a})₂ = carbocycle; R₈ = R, halo, OR, COR, CO₂R, COCOR, NO₂, CN, SO₀₋₂R, N(R₄)₂, CON(R₄)₂, SO₂(R₄)₂, OCOR, NR₄COR, NR₄CO₂(aliph.), NR₄N(R₄)₂, C:NN(R₄)₂, C:NOR, NR₄CO(R₄)₂, NR₄SO₂N(R₄)₂, NR₄SO₂R, or OCON(R₄)₂] were prepd. I are protein kinase inhibitors, esp. of Aurora-2 and GSK-3. For example, the (pyrazolylamino)quinazoline II was refluxed with thiophenol in t-BuOH to give III. In bioassays, I inhibited the following kinases with Ki values reported < 20 .mu.M: GSK-3.beta. (232 compds.), AURORA-2 (227 compds.), CDK-2 (13 compds.), ERK2 (8 compds.), AKT (10 compds.), and Human Src kinase (183 compds.). I are useful for the treatment of diseases assocd. with protein kinases, such as diabetes, cancer, and Alzheimer's disease (no data).

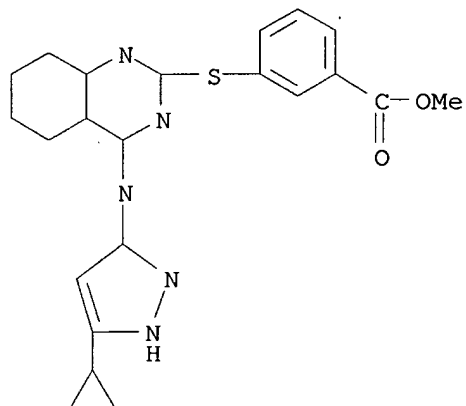
IT **438203-20-4P**, (5-Cyclopropyl-1H-pyrazol-3-yl)[2-(3-methoxycarbonylphenylsulfanyl)quinazolin-4-yl]amine **438203-23-7P**, [2-(4-Acetamidophenylsulfanyl)-7-methoxyquinazolin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-25-9P**, [2-(4-Acetamidophenylsulfanyl)-7-hydroxyquinazolin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-28-2P**, [2-(4-Acetamidophenylsulfanyl)-7-nitroquinazolin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-38-4P**, [2-(4-Acetamidophenylsulfanyl)-6-(4-methoxyphenyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438203-43-1P**, [6-Methoxycarbonyl-2-(4-propionylaminophenylsulfanyl)pyrimidin-4-yl](5-methyl-1H-pyrazol-3-yl)amine **438204-86-5P** **438204-90-1P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; prepn. of (pyrimidinylamino)pyrazoles as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 438203-20-4 CAPLUS

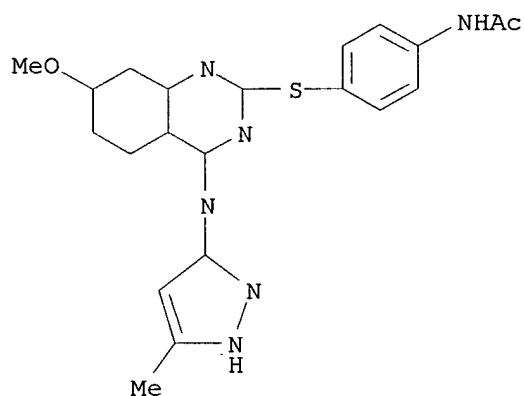
CN Benzoic acid, 3-[[4-[(5-cyclopropyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]thio]-, methyl ester (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 438203-23-7 CAPLUS

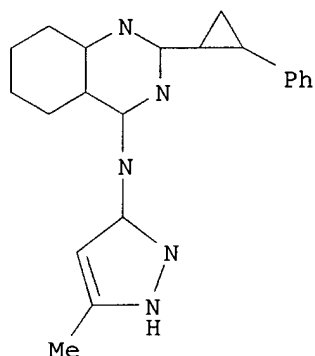
CN Acetamide, N-[4-[[7-methoxy-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]thio]phenyl]- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 438203-25-9 CAPLUS

CN Acetamide, N-[4-[[7-hydroxy-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-quinazolinyl]thio]phenyl]- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

L4 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:220584 CAPLUS

DOCUMENT NUMBER: 136:247584

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Bebbington, David; Knegt, Ronald; Golec, Julian M. C.; Li, Pan; Davies, Robert; Charrier, Jean-Damien

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 356 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

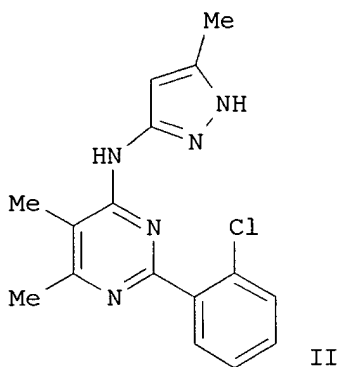
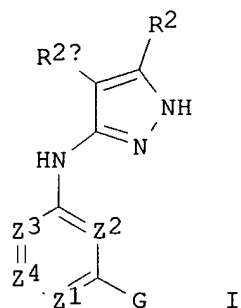
FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022608	A1	20020321	WO 2001-US42152	20010914
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001096871	A5	20020326	AU 2001-96871	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914
PRIORITY APPLN. INFO.:			US 2000-232795P	P 20000915
			US 2000-257887P	P 20001221
			US 2001-286949P	P 20010427
			WO 2001-US42152	W 20010914

OTHER SOURCE(S): MARPAT 136:247584

GI



AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR₉; Z2 = N or CH; Z3 = N or CR_x; Z4 = N or CR_y; R_x and R_y = independently TR₃, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2S0-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliph.), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliph. group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 = CR₉; Z2 and Z3 = N; Z4 = CR_y]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK-.beta.3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepd. and exhibited K_i values of < 0.1 .mu.M for glycogen synthetase kinase 3.beta. (GSK-3.beta.) and 0.1-1.0 .mu.M for Aurora-2.

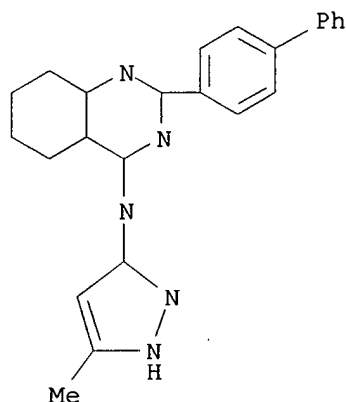
IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

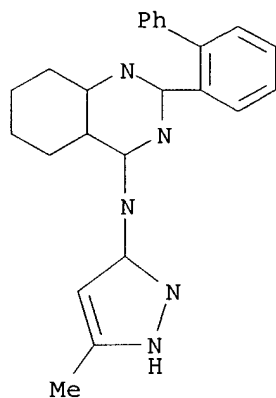
IT **404826-70-6P**, (2-Biphenyl-2-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; prepn. of heterocyclpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-70-6 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:220583 CAPLUS

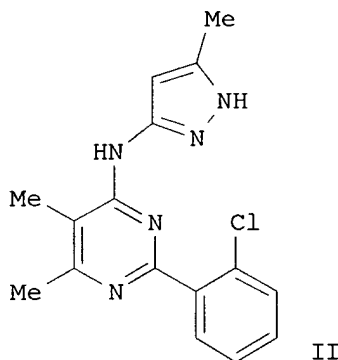
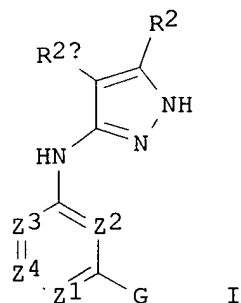
DOCUMENT NUMBER: 136:247583

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Davies, Robert; Bebbington, David; Knegetel, Ronald;
Wannamaker, Marion; Li, Pan; Forester, Cornelia;
Pierce, Albert; Kay, David
PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
SOURCE: PCT Int. Appl., 373 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 14
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022607	A1	20020321	WO 2001-US28940	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001091013	A5	20020326	AU 2001-91013	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914
PRIORITY APPLN. INFO.:			US 2000-232795P	P 20000915
			US 2000-257887P	P 20001221
			US 2001-286949P	P 20010427
			WO 2001-US28940	W 20010914

OTHER SOURCE(S): MARPAT 136:247583
GI



AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or

alkylidene chain; W = C(R6)2O, C(R6)2S0-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliph.), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliph. group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 and Z2 = N; Z3 = CRx; Z4 = CRY; G = Ring C]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK-.beta.3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepd. and exhibited Ki values of < 0.1 .mu.M for glycogen synthetase kinase 3.beta. (GSK-3.beta.) and 0.1-1.0 .mu.M for Aurora-2.

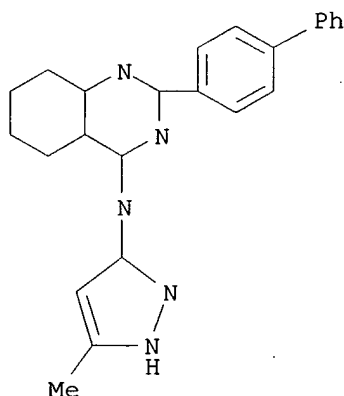
IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

IT **404826-70-6P**, (2-Biphenyl-2-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine **404873-55-8P** **404873-56-9P**

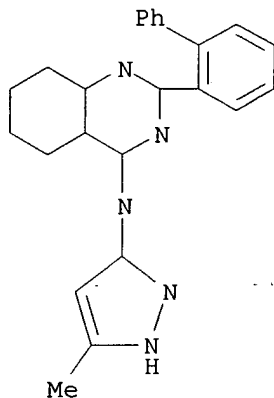
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes,

and Alzheimer's disease)

RN 404826-70-6 CAPLUS

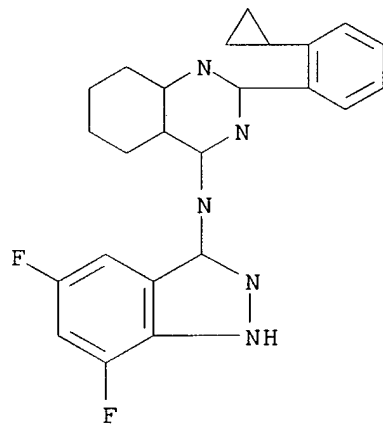
CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-
(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 404873-55-8 CAPLUS

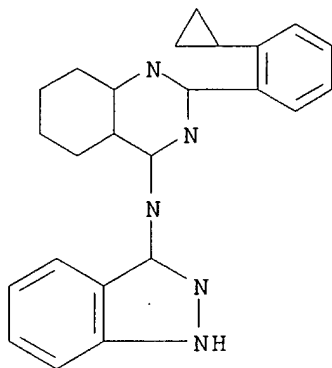
CN 4-Quinazolinamine, 2-(2-cyclopropylphenyl)-N-(5,7-difluoro-1H-indazol-3-yl)-
(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 404873-56-9 CAPLUS

CN 4-Quinazolinamine, 2-(2-cyclopropylphenyl)-N-1H-indazol-3-yl- (9CI) (CA
INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:220582 CAPLUS

DOCUMENT NUMBER: 136:247582

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Bebbington, David; Binch, Hayley; Knegt, Ronald; Golec, Julian M. C.; Patel, Sanjay; Charrier, Jean-Damien; Kay, David; Davies, Robert; Li, Pan; Wannamaker, Marion; Forster, Cornelia; Pierce, Albert

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 355 pp.

CODEN: PIXXD2

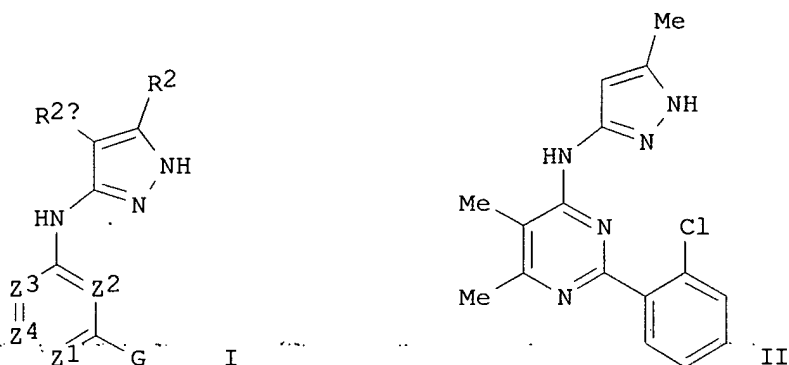
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022606	A1	20020321	WO 2001-US28803	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001090944	A5	20020326	AU 2001-90944	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914
PRIORITY APPLN. INFO.:			US 2000-232795P	P 20000915
			US 2000-257887P	P 20001221
			US 2001-286949P	P 20010427
			WO 2001-US28803	W 20010914
OTHER SOURCE(S):			MARPAT 136:247582	
GI				



AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliph.), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliph. group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (pyrimidinyl)pyrazolamines and indazolamines I [wherein Z1 and Z2 = N; Z3 = CRx; Z4 = CRy; G = Ring D]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK-3 β , Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepd. and exhibited Ki values of < 0.1 μ M for glycogen synthetase kinase 3 β . (GSK-3 β .) and 0.1-1.0 μ M for Aurora-2.

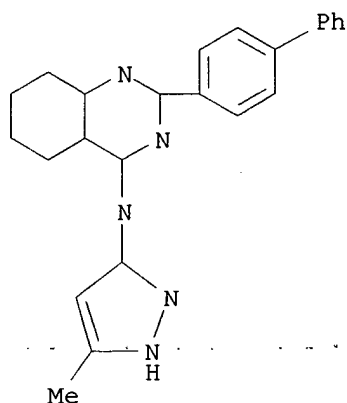
IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-
(9CI) (CA INDEX NAME)



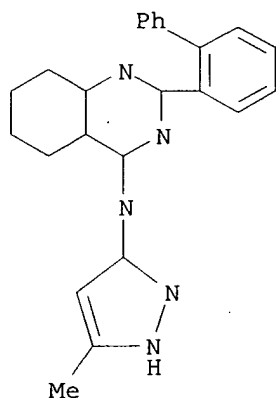
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IT **404826-70-6P**, (2-Biphenyl-2-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-70-6 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-
(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:220581 CAPLUS

DOCUMENT NUMBER: 136:247581

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Golec, Julian M. C.; Charrier, Jean-Damien; Knegt, Ronald; Bebbington, David; Davies, Robert; Li, Pan

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 357 pp.
CODEN: PIXXD2

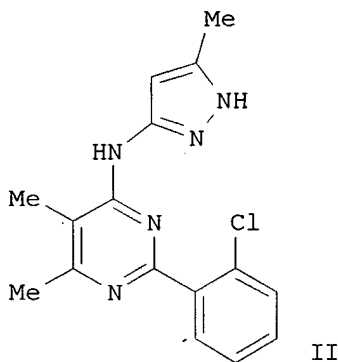
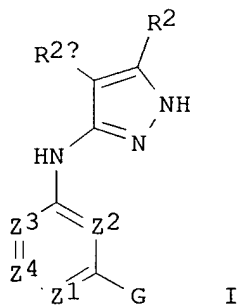
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022605	A1	20020321	WO 2001-US28793	20010914
W: AE, AG, AL, AM, AT, AU, AZ; BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001092670	A5	20020326	AU 2001-92670	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914
PRIORITY APPLN. INFO.:			US 2000-232795P	P 20000915
			US 2000-257887P	P 20001221
			US 2001-286949P	P 20010427
			WO 2001-US28793	W 20010914
OTHER SOURCE(S):			MARPAT 136:247581	
GI				



AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3

= N or CR_x; Z₄ = N or CR_y; R_x and R_y = independently TR₃, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R₂ and R_{2a} = independently R, TWR₆; or C₂R₂R_{2a} = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R₆)₂O, C(R₆)₂SO-₂, C(R₆)₂NR₆, CO, CO₂, CR₆OCO, CR₆OCONR₆, C(R₆)₂NR₆CO, C(R₆)₂NR₆CO₂, CR₆:NNR₆, CR₆:NO, C(R₆)₂NR₆NR₆, C(R₆)₂NR₆SO₂NR₆, C(R₆)₂NR₆CONR₆, or CONR₆; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R₃ = R, halo, O, OR, COR, CO₂R, COCOR, COCH₂COR, NO₂, CN, SO₀₋₂R, N(R₄)₂, CON(R₄)₂, SO₂N(R₄)₂, OCOR, NR₄COR, NR₄CO₂(aliph.), NR₄N(R₄)₂, C:NN(R₄)₂, C:NOR, NR₄CO(R₄)₂, NR₄SO₂N(R₄)₂, NR₄SO₂R, or OCON(R₄)₂; R₄ = R₇, COR₇, CO₂(aliph.), CON(R₇)₂, or SO₂R₇; or N(R₄)₂ = heterocyclyl or heteroaryl; R₆ and R₇ = independently H or (un)substituted aliph. group; or N(R₆)₂ = heterocyclyl or heteroaryl; or N(R₇)₂ = heterocyclyl or heteroaryl; R₉ = R, halo, OR, COR, CO₂R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover pyrazolamines and indazolamines I [wherein Z₁ = N or CR₉; Z₂ = N or CH; Z₃ = N or CR_x; Z₄ = N; at least one of Z₁ or Z₃ = N]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK-3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepd. and exhibited K_i values of < 0.1 .mu.M for glycogen synthetase kinase 3.beta. (GSK-3.beta.) and 0.1-1.0 .mu.M for Aurora-2.

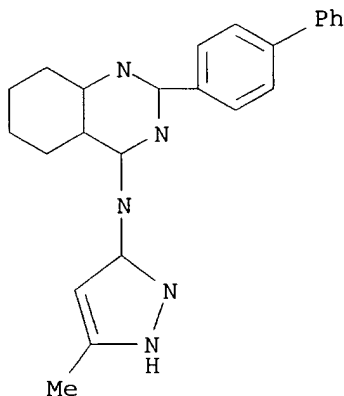
IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

IT **404826-70-6P**, (2-Biphenyl-2-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

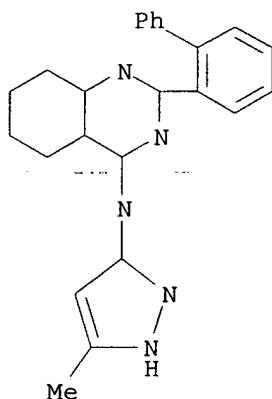
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; prepn. of heterocyclpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-70-6 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:220580 CAPLUS

DOCUMENT NUMBER: 136:247606

TITLE: Preparation of 3-(4-pyrimidinylamino)pyrazole derivatives as protein kinase inhibitors, especially of Aurora-2 and GSK-3, for treating cancer, diabetes and Alzheimer's disease.

INVENTOR(S): Davies, Robert; Bebbington, David; Binch, Haley; Knegetel, Ronald; Golec, Julian M. C.; Patel, Sanjay; Charrier, Jean-Damien; Kay, David; Davies, Robert

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 357 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022604	A1	20020321	WO 2001-US28792	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001094558 A5 20020326

AU 2001-94558 20010914

US 2003055044 A1 20030320

US 2001-953505 20010914

PRIORITY APPLN. INFO.:

US 2000-232795P P 20000915

US 2000-257887P P 20001221

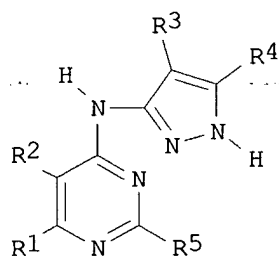
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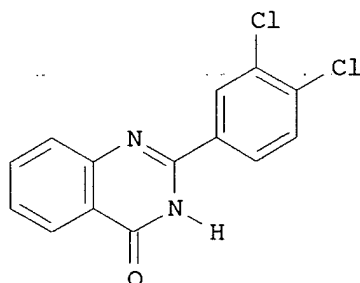
OTHER SOURCE(S):

MARPAT 136:247606

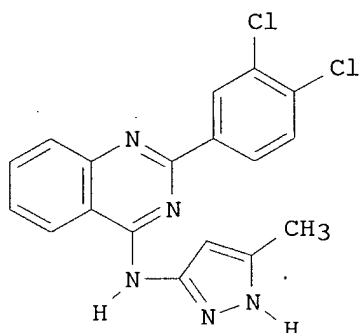
GI



I



II



III

AB The prepn. of title compds. I and their pharmaceutically acceptable salts or prodrugs is described [wherein: R1, R2 = dependently form (un)substituted fused, unsatd. or partially unsatd., 5-8 membered carbocyclo ring; R3, R4 = independently H, aliph., aryl, heteroaryl, heterocyclyl, or wide variety of functionalized sidechains; or dependently form a fused, 5-8 membered, unsatd. or partially unsatd. ring having 0-3 ring heteroatoms (N, S, O); R5 = fused, (un)substituted 5-7 membered monocyclic ring or 8-10 membered bicyclic ring (aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms (N, S, O))]. For example, chlorination of quinazolinone II with phosphorus oxychloride, followed by condensation with 3-amino-5-methylpyrazole afforded claimed compd. III. Compds. I are inhibitors of GSK-3 and Aurora-2 protein kinases. The invention also relates to methods of treating diseases assocd. with these protein kinases, such as diabetes, cancer and Alzheimer's disease. In bioassays, compds. I inhibited the following kinases with Kis reported < 100 nM: GSK-3.beta. (163 compds.), AURORA-2 (65 compds.), CDK-2 (no data), ERK2 (8 compds.), AKT (no data), and Human Src kinase (21 compds.). Claims

included 146 specific compds., and 188 examples were given. The syntheses of 6 compds. and 46 intermediates are described.

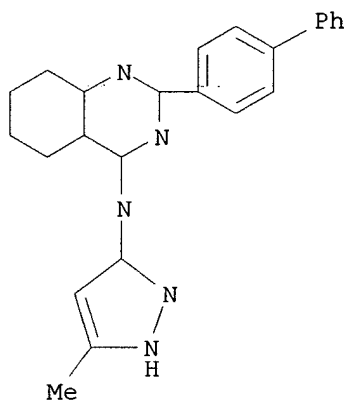
IT 404826-22-8P 404826-70-6P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 3-(4-pyrimidinylamino)pyrazole compds. as protein kinase inhibitors)

RN 404826-22-8 CAPLUS

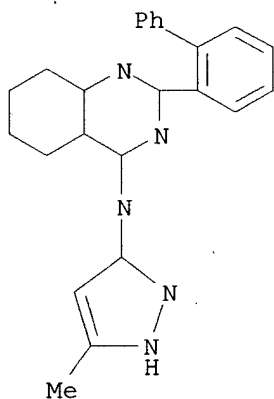
CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 404826-70-6 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

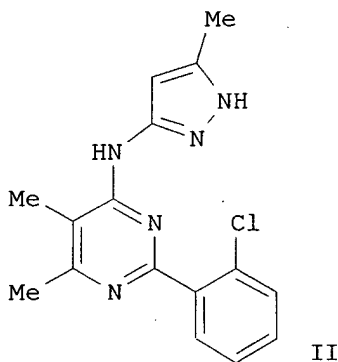
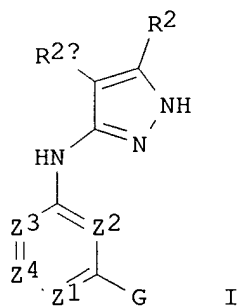
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:220579 CAPLUS

DOCUMENT NUMBER: 136:247580
 TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease
 INVENTOR(S): Davies, Robert; Li, Pan; Golec, Julian; Bebbington, David
 PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA
 SOURCE: PCT Int. Appl., 406 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 14
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022603	A1	20020321	WO 2001-US28738	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001090912	A5	20020326	AU 2001-90912	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914
PRIORITY APPLN. INFO.:			US 2000-232795P	P 20000915
			US 2000-257887P	P 20001221
			US 2001-286949P	P 20010427
			WO 2001-US28738	W 20010914
OTHER SOURCE(S):			MARPAT 136:247580	
GI				



AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl,

heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2SO-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliph.), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliph. group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 = R, halo, OR, COR, CO2R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (triazinyl)pyrazolamines and indazolamines I [wherein Z1, Z2, and Z3 = N; Z4 = CRy]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK-.beta.3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepd. and exhibited Ki values of < 0.1 .mu.M for glycogen synthetase kinase 3.beta. (GSK-3.beta.) and 0.1-1.0 .mu.M for Aurora-2.

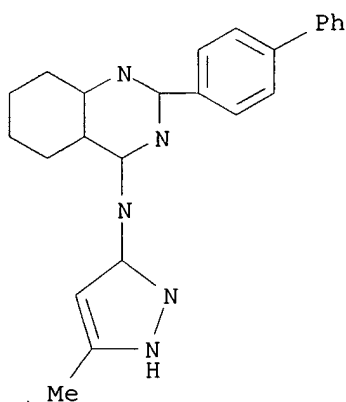
IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)- (9CI) (CA INDEX NAME)



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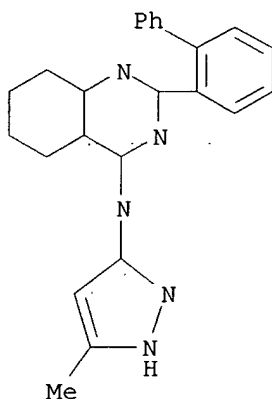
IT **404826-70-6P**, (2-Biphenyl-2-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; prepn. of heterocyclpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-70-6 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:220578 CAPLUS

DOCUMENT NUMBER: 136:263164

TITLE: Preparation of triazolamines as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Bebbington, David; Knegt, Ronald; Binch, Haley; Golec, Julian M. C.; Li, Pan; Charrier, Jean-Damien

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 377 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022602	A2	20020321	WO 2001-US42162	20010914
WO 2002022602	A3	20020627		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001096875 A5 20020326

AU 2001-96875 20010914

US 2003055044 A1 20030320

US 2001-953505 20010914

PRIORITY APPLN. INFO.:

US 2000-232795P P 20000915

US 2000-257887P P 20001221

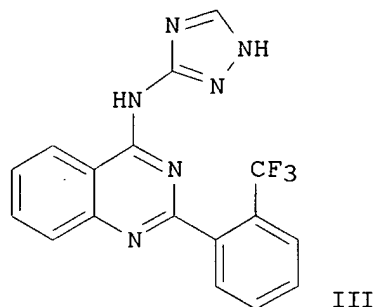
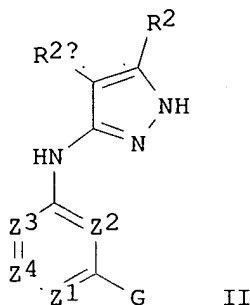
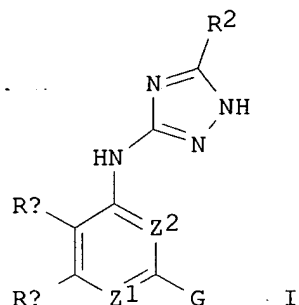
US 2001-286949P P 20010427

WO 2001-US42162 W 20010914

OTHER SOURCE(S):

MARPAT 136:263164

GI



AB Triazolamines I and pyrazolamines II [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR9; Z2 = N or CH; Z3 = N or CRx; Z4 = N or CRy; Rx and Ry = independently TR3, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R2 and R2a = independently R, TWR6; or C2R2R2a = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R6)2O, C(R6)2S0-2, C(R6)2NR6, CO, CO2, CR6OCO, CR6OCONR6, C(R6)2NR6CO, C(R6)2NR6CO2, CR6:NNR6, CR6:NO, C(R6)2NR6NR6, C(R6)2NR6SO2NR6, C(R6)2NR6CONR6, or CONR6; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R3 = R, halo, O, OR, COR, CO2R, COCOR, COCH2COR, NO2, CN, SO0-2R, N(R4)2, CON(R4)2, SO2N(R4)2, OCOR, NR4COR, NR4CO2(aliph.), NR4N(R4)2, C:NN(R4)2, C:NOR, NR4CO(R4)2, NR4SO2N(R4)2, NR4SO2R, or OCON(R4)2; R4 = R7, COR7, CO2(aliph.), CON(R7)2, or SO2R7; or N(R4)2 = heterocyclyl or heteroaryl; R6 and R7 = independently H or (un)substituted aliph. group; or N(R6)2 = heterocyclyl or heteroaryl; or N(R7)2 = heterocyclyl or heteroaryl; R9 =

R, halo, OR, COR, CO₂R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover (heterocyclyl)triazolamines I [wherein Z1 = N or CR9; Z2 = N or CH; R9 is defined above]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK- β , Aurora-2, ERK, and Src. For instance, the N-(4-quinazolinyl)-1H-1,2,4-triazol-3-amine III was prepd. and exhibited K_i values of < 0.1 μ M for glycogen synthetase kinase 3 β (GSK-3 β) and 1.0-20 μ M for Aurora-2.

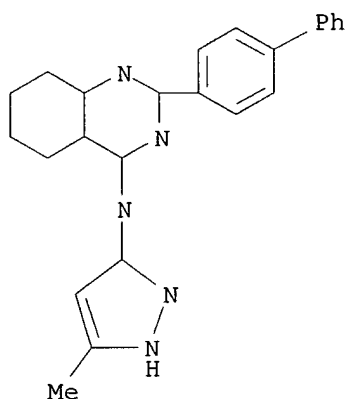
IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; prepn. of triazolamines, pyrazolamines, and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



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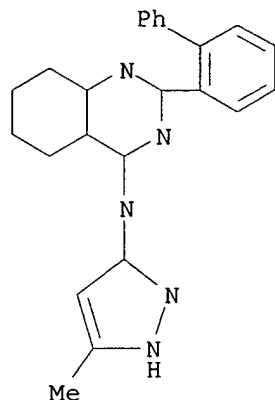
IT **404826-70-6P**, (2-Biphenyl-2-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(protein kinase inhibitor; prepn. of triazolamines, pyrazolamines, and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-70-6 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-(9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

L4 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:220577 CAPLUS

DOCUMENT NUMBER: 136:247579

TITLE: Preparation of pyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease

INVENTOR(S): Knegtel, Ronald; Bebbington, David; Binch, Hayley; Golec, Julian; Patel, Sanjay; Charrier, Jean-Damien; Kay, David; Davies, Robert; Li, Pan; Wannamaker, Marion; Forster, Cornelia; Pierce, Albert

PATENT ASSIGNEE(S): Vertex Pharmaceuticals Incorporated, USA

SOURCE: PCT Int. Appl., 376 pp.

CODEN: PIXXD2

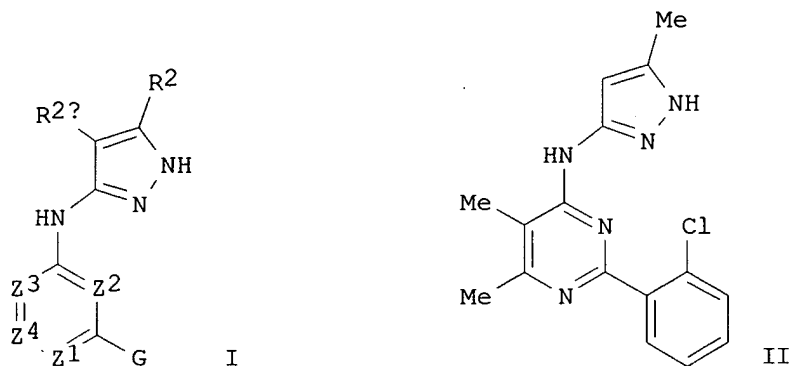
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022601	A1	20020321	WO 2001-US28740	20010914
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001090914	A5	20020326	AU 2001-90914	20010914
US 2003055044	A1	20030320	US 2001-953505	20010914
PRIORITY APPLN. INFO.:			US 2000-232795P	P 20000915
			US 2000-257887P	P 20001221
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			WO 2001-US28740	W 20010914
OTHER SOURCE(S):			MARPAT 136:247579	
GI				



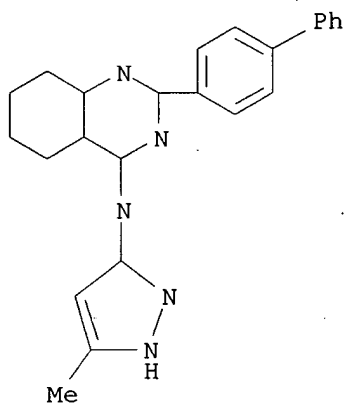
AB Title compds. I [wherein G = Ring C or Ring D; Ring C = (un)substituted Ph, pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, or 1,2,4-triazinyl; Ring D = (un)substituted monocyclic or bicyclic ring selected from aryl, heteroaryl, heterocyclyl, or carbocyclyl; Z1 = N or CR₉; Z2 = N or CH; Z3 = N or CR_x; Z4 = N or CR_y; R_x and R_y = independently TR₃, or taken together with their intervening atoms form an (un)satd. fused ring having 1-3 ring heteroatoms; R₂ and R_{2a} = independently R, TWR₆; or C₂R₂R_{2a} = (un)substituted fused ring contg. 0-3 heteroatoms; T = a bond or alkylidene chain; W = C(R₆)₂O, C(R₆)₂SO-2, C(R₆)₂NR₆, CO, CO₂, CR₆OCO, CR₆OCONR₆, C(R₆)₂NR₆CO, C(R₆)₂NR₆CO₂, CR₆:NNR₆, CR₆:NO, C(R₆)₂NR₆NR₆, C(R₆)₂NR₆SO₂NR₆, C(R₆)₂NR₆CONR₆, or CONR₆; R = H or (un)substituted aliph., (hetero)aryl, or heterocyclyl ring; R₃ = R, halo, O, OR, COR, CO₂R, COCOR, COCH₂COR, NO₂, CN, SO₀-2R, N(R₄)₂, CON(R₄)₂, SO₂N(R₄)₂, OCOR, NR₄COR, NR₄CO₂(aliph.), NR₄N(R₄)₂, C:NN(R₄)₂, C:NOR, NR₄CO(R₄)₂, NR₄SO₂N(R₄)₂, NR₄SO₂R, or OCON(R₄)₂; R₄ = R₇, COR₇, CO₂(aliph.), CON(R₇)₂, or SO₂R₇; or N(R₄)₂ = heterocyclyl or heteroaryl; R₆ and R₇ = independently H or (un)substituted aliph. group; or N(R₆)₂ = heterocyclyl or heteroaryl; or N(R₇)₂ = heterocyclyl or heteroaryl; R₉ = R, halo, OR, COR, CO₂R, COCOR, etc.] were prepd. as protein kinase inhibitors, esp. as inhibitors of Aurora-2 and GSK-3, for treating diseases such as cancer, diabetes, and Alzheimer's disease. Claims cover pyrimidinyl- and pyridinyl- pyrazolamines and indazolamines I [wherein Z1 = N, CR_a, or CH; Z2 = N or CH; and at least one of Z1 or Z2 = N; Z3 = CR_x; Z4 = CR_y; R_a = halo, OR, COR, CO₂R, COCOR, NO₂, CN, SO₀-2R, N(R₄)₂, CON(R₄)₂, SO₂N(R₄)₂, OCOR, NR₄COR, etc.; R and R₄ are defined above]. Examples include data for approx. 300 invention compds. prepd. by a variety of synthetic methods and bioassay results for the inhibition of GSK-3, Aurora-2, ERK, and Src. For instance, the N-(4-pyrimidinyl)-3-pyrazolamine II was prepd. and exhibited K_i values of < 0.1 .mu.M for glycogen synthetase kinase 3.beta. (GSK-3.beta.) and 0.1-1.0 .mu.M for Aurora-2.

IT **404826-22-8P**, (2-Biphenyl-4-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(protein kinase inhibitor; prepn. of heterocyclylpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-22-8 CAPLUS

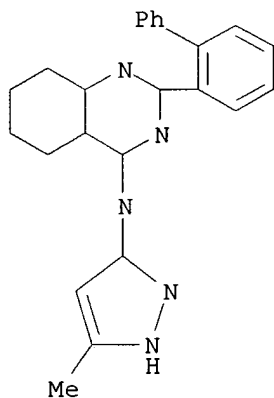
CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-4-yl-N-(5-methyl-1H-pyrazol-3-yl)-
(9CI) (CA INDEX NAME)

*** FRAGMENT DIAGRAM IS INCOMPLETE ***

IT 404826-70-6P, (2-Biphenyl-2-ylquinazolin-4-yl) (5-methyl-2H-pyrazol-3-yl)amine

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(protein kinase inhibitor; prepn. of heterocyclpyrazolamines and analogs as protein kinase inhibitors for treatment of cancer, diabetes, and Alzheimer's disease)

RN 404826-70-6 CAPLUS

CN 4-Quinazolinamine, 2-[1,1'-biphenyl]-2-yl-N-(5-methyl-1H-pyrazol-3-yl)-
(9CI) (CA INDEX NAME)

*** FRAGMENT DIAGRAM IS INCOMPLETE ***

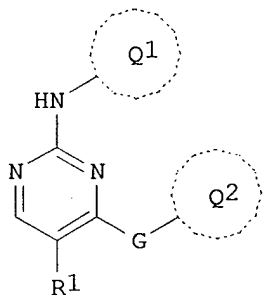
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2003 ACS

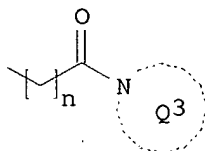
ACCESSION NUMBER: 2001:661403 CAPLUS

DOCUMENT NUMBER: 135:227010
 TITLE: Preparation of 2,4-di(hetero)arylamino(oxy)-5-substituted pyrimidines as antineoplastic agents
 INVENTOR(S): Pease, Elizabeth Janet; Breault, Gloria Anne; Williams, Emma Jane; Bradbury, Robert Hugh; Morris, Jeffrey James
 PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca UK Limited
 SOURCE: PCT Int. Appl., 74 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

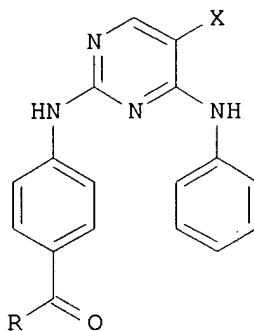
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064655	A1	20010907	WO 2001-GB824	20010226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG BR 2001008834 A 20021210 BR 2001-8834 20010226 EP 1268444 A1 20030102 EP 2001-906018 20010226 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR NO 2002004153 A 20021029 NO 2002-4153 20020830 PRIORITY APPLN. INFO.: GB 2000-4890 A 20000301 WO 2001-GB824 W 20010226 OTHER SOURCE(S): MARPAT 135:227010 GI				



I



II



III

AB The title compds. [I; Q1, Q2 = (un)substituted aryl or carbon linked heteroaryl; and one or both Q1 and Q2 are substituted on a ring carbon by (CH2)nY(CH2)mZ or II (Y = NHCO, CONH; Z = (un)substituted cycloalkyl, Ph,

heterocyclyl, etc.; n = 0-1; m = 1-3; Q3 = (un)substituted nitrogen linked heterocycle); G = O, NR₂; R₂ = H, alkyl, alkenyl, etc.; R₁ = H, halo, OH, etc.] and their pharmaceutically acceptable salts, useful as cyclin-dependent serine/threonine kinase (CDK) and focal adhesion kinase (FAK) inhibitors, were prepd. and formulated. Thus, reacting 4-anilino-2,5-dichloropyrimidine with 4-aminobenzoic acid followed by amidation of the resulting 4-anilino-2-(4-carboxyanilino)-5-chloropyrimidine with 1-(3-aminopropyl)imidazole afforded III [X = Cl; R = 3-(imidazol-1-yl)propylamino]. E.g., the title compd. III [X = Br; R = 2-(piperidino)ethylamino] showed IC₅₀ of 0.235 .mu.M when tested in vitro assay for the CDK4 inhibitory activity.

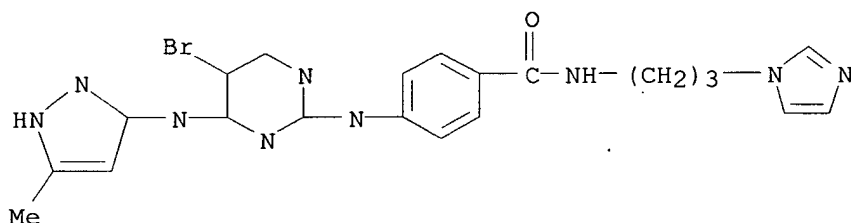
IT 358789-01-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 2,4-di(hetero)arylamino(oxy)-5-substituted pyrimidines as antineoplastic agents)

RN 358789-01-2 CAPLUS

CN Benzamide, 4-[[5-bromo-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]amino]-N-[3-(1H-imidazol-1-yl)propyl]- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:617995 CAPLUS

DOCUMENT NUMBER: 135:180783

TITLE: Preparation of arylaminopyrimidines as Kinase inhibitors

INVENTOR(S): Armistead, David M.; Bemis, Jean E.; Di Pietro, Lucian V.; Geuns-Meyer, Stephanie D.; Habgood, Gregory J.; Kim, Joseph L.; Nunes, Joseph J.; Patel, Vinod F.; Toledo-Sherman, Leticia M.

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: PCT Int. Appl., 91 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

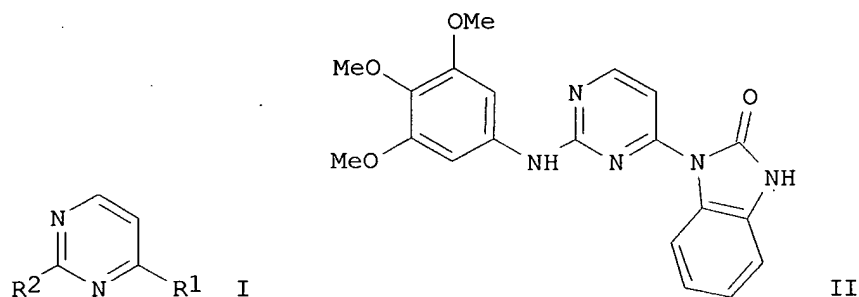
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060816	A1	20010823	WO 2001-US4983	20010216
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
 SD, SE, SG
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 US 2002052386 A1 20020502 US 2001-785599 20010216
 US 20030004174 A9 20030102
 EP 1257546 A1 20021120 EP 2001-909266 20010216
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 PRIORITY APPLN. INFO.: US 2000-183256P P 20000217
 WO 2001-US4983 W 20010216
 OTHER SOURCE(S): MARPAT 135:180783
 GI



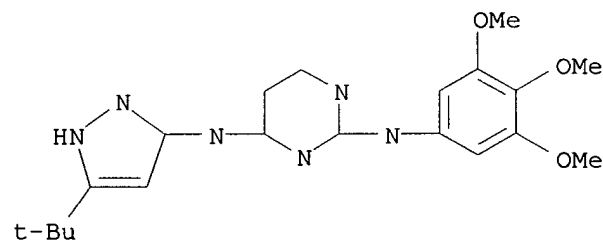
AB Arylamino pyrimidines I wherein R¹ and R² are independently aryl, 5-8 membered monocyclic, 11-14 membered bicyclic, 1-9-heteroatoms tricyclic, substituted amine, sulfide, alkoxy, acyl, heterocycle, were prepd. as Kinase inhibitors useful for treating disease or disease symptoms. Thus, pyrimidine II was prepd. and tested in vitro as kinases inhibitor (FGFR1-1, IC₅₀ < 1.5 .mu.M).

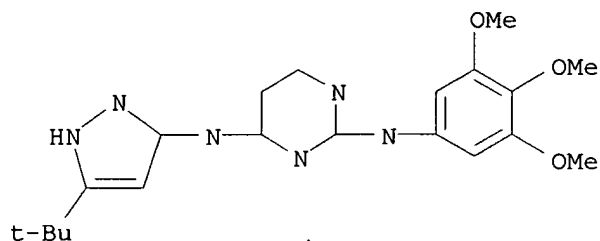
IT **354817-37-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (Prepn. of triazine Kinase inhibitors)

RN 354817-37-1 CAPLUS

CN 2,4-Pyrimidinediamine, N4-[5-(1,1-dimethylethyl)-1H-pyrazol-3-yl]-N2-(3,4,5-trimethoxyphenyl)- (9CI) (CA INDEX NAME)





*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:457043 CAPLUS

DOCUMENT NUMBER: 133:89537

TITLE: Preparation of 2,4-pyrimidinediamine derivatives as anticancer agents

INVENTOR(S): Bradbury, Robert Hugh; Breault, Gloria Anne; Jewsbury, Philip John; Pease, Janet Elizabeth

PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK

SOURCE: PCT Int. Appl., 137 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

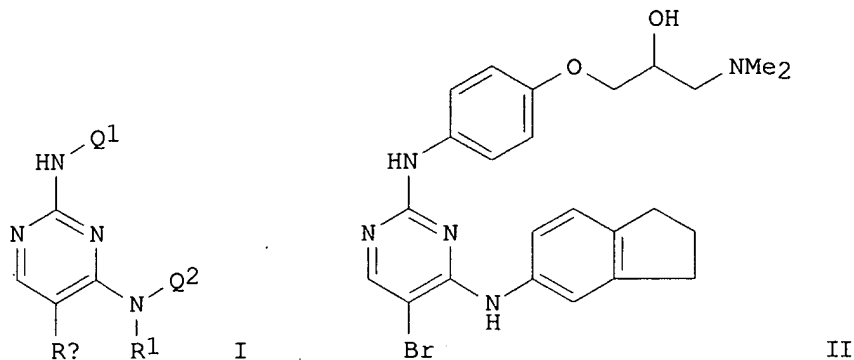
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039101	A1	20000706	WO 1999-GB4325	19991220
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RW:		GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
EP 1140860	A1	20011010	EP 1999-962375	19991220
R:		AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO		
BR 9916590	A	20011023	BR 1999-16590	19991220
JP 2002533446	T2	20021008	JP 2000-591012	19991220
NO 2001003038	A	20010822	NO 2001-3038	20010619
PRIORITY APPLN. INFO.:			GB 1998-28511	A 19981224
			WO 1999-GB4325	W 19991220

OTHER SOURCE(S): MARPAT 133:89537

GI



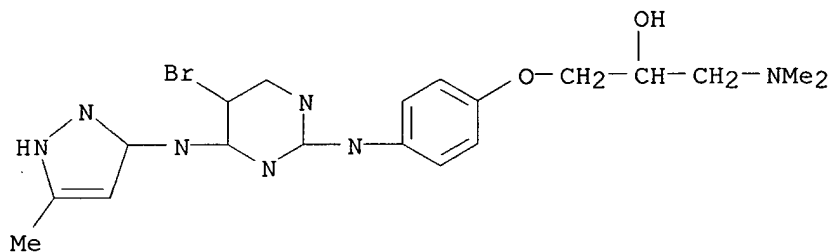
AB The present invention relates to the title compds. (I) [wherein R1 = H, (un)substituted alkyl, alkenyl, or alkynyl, benzyl, 2-phenylethyl, phthalimidoalkyl, or cycloalkylalkyl; Rx = halo, OH, NO2, NH2, CN, SH, CO2H, SO2NH2, NHCHO, ureido, etc.; Q1 and Q2 = independently (un)substituted aryl, 5- or 6-membered monocycle, or 9- or 10-membered bicyclic heterocycle], processes for their manuf., and pharmaceutical compns. contg. them. For example, addn. of 4-[2-hydroxy-3-(N,N-dimethylamino)propoxy]aniline.bul.HCl in MeOH to 5-bromo-2-chloro-4-(indan-5-ylamino)pyrimidine in BuOH (prepn. given) and heating to 100.degree.C for 18 h gave II (42%). I inhibited the effects of cyclin-dependent serine/threonine kinases (CDKs), showing selectivity for CDK2 (no data), CDK4 (IC50 ranging from 0.02 .mu.M to 0.07 .mu.M), and CDK6 (no data). In a tyrosine kinase activity assay using Sf21 cells transfected with plaque-pure FAK recombinant virus, I also inhibited focal adhesion kinase 3 (FAK3) with IC50 ranging from 0.032 .mu.M to 0.07 .mu.M. Typical IC50 values for I when tested for inhibition of cell growth in an Sulforhodamine B (SRB) assay were in the range of 1 mM to 1 nM. Thus, I possess anti-cancer properties, including anti-cell-migration, antiproliferation and/or apoptotic properties. Such properties are expected to be of value in the treatment of disease states assocd. with aberrant cell cycles and cell proliferation such as cancers (solid tumors and leukemias), fibroproliferative and differentiative disorders, psoriasis, rheumatoid arthritis, Kaposi's sarcoma, hemangioma, acute and chronic nephropathies, atheroma, atherosclerosis, arterial restenosis, autoimmune diseases, acute and chronic inflammation, bone diseases, and ocular diseases with retinal vessel proliferation.

IT **280580-25-8P 280580-63-4P 280580-64-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2,4-pyrimidinediamine anticancer agents by coupling halopyrimidines with anilines and optional derivatization)

RN 280580-25-8 CAPLUS

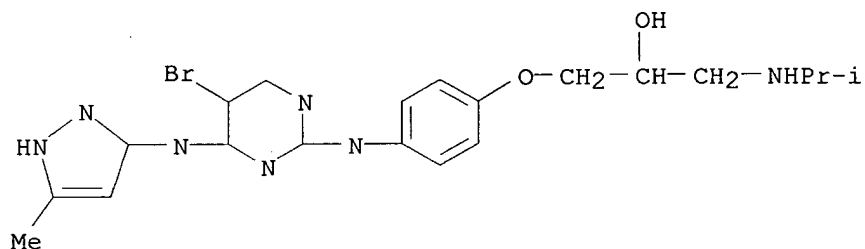
CN 2-Propanol, 1-[4-[[5-bromo-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]amino]phenoxy]-3-(dimethylamino)- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 280580-63-4 CAPLUS

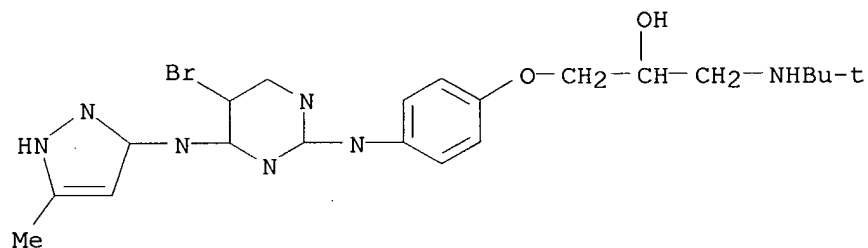
CN 2-Propanol, 1-[4-[[5-bromo-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]amino]phenoxy]-3-[(1-methylethyl)amino]- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

RN 280580-64-5 CAPLUS

CN 2-Propanol, 1-[4-[[5-bromo-4-[(5-methyl-1H-pyrazol-3-yl)amino]-2-pyrimidinyl]amino]phenoxy]-3-[(1,1-dimethylethyl)amino]- (9CI) (CA INDEX NAME)



*** FRAGMENT DIAGRAM IS INCOMPLETE ***

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS

FULL ESTIMATED COST

SINCE FILE

ENTRY

68.87

TOTAL

SESSION

217.23

Habte

3/28/2003

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-9.77	-9.77

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